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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/816,242	04/01/2004	James Freddo	PC25581A	9207

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PFIZER INC
10555 SCIENCE CENTER DRIVE
SAN DIEGO, CA 92121

EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
12/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/816,242	FREDDO ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,13,15,16,32,37,39-41 and 49-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8, 13, 15-16, 32, 37, 39-41 and 49-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

1. The amendment filed on 8/28/08 has been entered.

2. The arguments filed on **8/28/08** have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 8, 13, 15-16, 32, 37, 39-41 and 49-53 are pending in this office action.

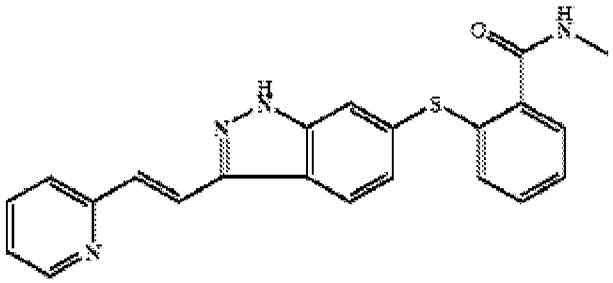
5. Claims 8, 13, 15-16, 32, 37, 39-41 and 49-53 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Kania et al. (WO 2001/02369 or US Patent 6,531,491) in view of Sweeney et al. (2001) further in view of Goodman and Gilman, for the reasons made of record in Paper No. 20080529, and as follows.

Applicant argues that: Kania discloses a broad range of about 0.001-about 50 mg/kg which translates to 0.08-4000 mg. Applicant then relies on Rugo et al., (Applicant's submission) that the teaching of phase I preclinical trial results of AG013736 shows dose limiting toxicity and maximum-tolerated dose of AG013736. Pages 2-7 of the response assert that the administration of 20 mg orally resulted in significant toxicity.

Lastly, Applicant argues that none of the references would result in the claim invention.

In response: Even though Kania teaches a very broad range as asserted by Applicant, Kania teaches that the actual dosages of the agents used will vary according to the particular complex employed, the particular formulation, mode of administration, and host and disease being treated (see col. 21, lines 22-35). It is further asserted that optimal dosages for a given set of conditions can be ascertained by those skilled in the art using conventional dosage determination test in view of experimental data for an agent. Based of the above teaching of Kania et al. one of ordinary skill in the art would have been motivated to try varying concentrations within the teaching, which still encompass the dosage claimed.

In contrast, the claims merely recite a dosage composition or a treatment method wherein the drug is employed with the cited dosage of 1-10 mg. With regards to the toxicity, this is not giving consideration because all drugs have side effects, and the rejection involves optimization of dosage as prima facie obvious. With regards to the Sweeney reference, it was introduce for its teaching of the inhibition of solid tumors by docetaxel when the proangiogenic factor is VEGF. It is noted that Kania teaches that the invention modulates and or inhibits the kinase activity of VEGF-R by administering compounds such as AG013736 as represented by the structure



. See col. 11, lines 34-36 and 12, lines 54-60. Therefore, one of ordinary skill in the art would know that combining two agents that has been used individually for the same purpose would result in additive or synergistic effect. The artisan would reasonably expect success in **enhancing the chemosensitivity of solid tumors with the compound of Kania, since the mechanism of both drugs involve VEGF kinase activity in solid tumors.** "[A] person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." *KSR Intemational Co. v. Teleflex Inc.,* 82 USPQ2d 1385, 1390.

The instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order form a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims, given the teaching of the prior art methods of using AG013736 and docetaxel individually for treating solid tumors, it would have been obvious to use both compounds for the treatment of solid tumors

because the idea of doing so would have logically followed from their having been individually taught in the prior art to be useful as therapeutic agents.

In summary the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Careful consideration has been given to Applicant's remarks and the Rugo reference, but they are not persuasive for the reasons given supra. The rejection is maintained as stated in the last office action of record.

6. Claims 8, 13, 15-16, 32, 37, 39-41 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1 - 11** of U.S. Patent **7141581**. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicant argues that the patent 7141581are directed to methods of treatment with various compounds and without any specific dosing range.

In response: claim 1 of the patent recites a therapeutically effective amount of a composition comprising compounds of formula 1 (see claim 1 of patent, col. 29, lines 46-60 wherein the cancers are selected from lung, pancreatic and skin cancers.

The claims recite a range, and one of ordinary skill in the art would have been motivated to optimize the dosage and administer an optimal dosage to the patient in need thereof. The specification of the patent, also, teaches an amount of a given agent that corresponds to the dosage range claimed in the instant application (see col. 25, lines 24-30). The amount will vary depending upon factors such as the particular compound, disease condition and its severity, the patient's age and weight of the mammal in need of treatment, but can nevertheless be routinely determined by one skilled in the in the art.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert C. Hayes/
Primary Examiner, Art Unit 1649

/S. V. G./
Examiner, Art Unit 1618
11/12/08